Effect of physicochemical properties of lubricants on dissolution behavior of acetaminophen from tablet

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In solid pharmaceutical formulations, magnesium stearate (Mg-St), which is widely used as a hydrophobic lubricant, is considered to cause retardation of drug dissolution. Recently, we demonstrated that glycerin fatty acid ester (Poem TR-FB®, TR-FB) did not cause a retardation of drug dissolution and that the differences in dissolution rate as well as dissolution behavior could be explained using an analysis of available surface area $S(t)$. Since some conventional lubricants such as sodium stearyl fumarate (SSF) and talc are different from Mg-St or TR-FB in physicochemical properties, effect of physicochemical properties of lubricants on dissolution behavior of drug is considered to be different in these lubricants. In this study, the dissolution behavior of acetaminophen (APAP) from tablet formulated with various lubricants was examined using the analysis of $S(t)$.

In the dissolution tests, a retarded dissolution of APAP was not observed for TR-FB, SSF and talc, whereas Mg-St retarded the dissolution. With regard to the time course of the $S(t)$, the profiles for APAP with Mg-St at greater than 0.5% showed downward curvature, indicating a gradual decrease in surface area over time. Conversely, with TR-FB, SSF, and talc, even when its concentration was increased, the $S(t)$ profile for APAP had a maximum value which was more than twice that with Mg-St at 0.5-3.0%. In order to evaluate the effect of lubricant on tablet wettability, contact angle of drop of water and time required to absorb the drop of water into tablet (t_{absorb}) were measured. The contact angle was larger for TR-FB than that for Mg-St, and those for SSF and talc were smaller than that for Mg-St. However, for TR-FB, t_{absorb} was shorter than that for Mg-St. Scanning electron microscopic observations showed the morphological differences in the extensibility of these lubricants, which could explain the differences in their dissolution rates and $S(t)$ patterns. Principal component analysis showed that the differences for these lubricants in dissolution rate was related to its $S(t)$, contact angle, and t_{absorb}. In conclusion, the analysis of available surface area could be a useful tool to distinguish dissolution behavior of acetaminophen from tablet.